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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,583	08/31/2001	Andrew Robinson	1581.0840001/RWE	9616

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EXAMINER

MINNIFIELD, NITA M

ART UNIT PAPER NUMBER

1645

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/942,583	ROBINSON ET AL	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 October 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 22 and 23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 22 and 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) <u>7 page</u> | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>10/28/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 28, 2004 has been entered.

2. Applicants' amendment filed October 28, 2004 is acknowledged and has been entered. Claims 9-21, 24 and 25 have been canceled. Claims 1-8, 22 and 23 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment and/or comments with the exception of those discussed below. This is a NON-FINAL Office Action.

3. The terminal disclaimer filed on October 28, 2004 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of 10/185769 has been reviewed and is accepted. The terminal disclaimer has been recorded.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. It is noted that the effective filing date for the claimed invention is August 31, 2001. Applicants' priority documents (PCT/GB00/00624, United Kingdom 9904028.9 and United Kingdom 9922561.7) have been reviewed. The claimed method was first disclosed and enabled in the pending application 09/942583, filed August 31, 2001.

8. Claims 1-8, 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over van der Ley et al (Infection and Immunity, 1992, 60/8:3156-3161), Liljeqvist et al (J. Biotechnology, 1999, 73:1-33), Galen (6413768), Graham et al (6534638) or Blake et al (6013267).

The claims are directed to a method of preparing a composition, said composition comprising an isolated heterologous gene product and a pharmaceutically acceptable carrier, said method comprising the steps of: (a) inserting a gene coding for the heterologous gene product into an expression vector; (b) transforming said expression vector into a commensal *Neisseria*; (c) expressing said heterologous gene product in said commensal *Neisseria*; (d) isolating said heterologous gene product from the *Neisseria* of (c); and (e) combining the heterologous gene product of (d) with the pharmaceutically acceptable carrier, wherein said heterologous gene product is selected from (1) a product of a gene of a non-*Neisserial* organism and (2) a product of a gene of a pathogenic *Neisseria*.

Van der Ley teaches methods of preparing a composition comprising an outer membrane protein from *Neisseria meningitis* (i.e. heterologous protein) and a pharmaceutically acceptable carrier (abstract). The prior art teaches the insertion of a class 1 gene (class 1 outer membrane protein) into plasmid vector (i.e. expression vector), transforming the expression vector into a bacterial host and expressing the outer membrane protein (materials and methods, pp. 3156-3157). van der Ley et al teaches methods of isolating the outer membrane protein and that the isolated proteins were used in a composition comprising the protein and saline or aluminum phosphate (i.e. pharmaceutically acceptable carrier) (materials and methods, p. 3157).

Liljeqvist et al teaches the preparation and use of recombinant subunit vaccine compositions (p. 2). The prior art teaches that “[M]olecular biology and genetic engineering have provided vaccine development with valuable tools for recombinant protein production, which enables single proteins to be easily produced in various hosts, with multiple possibilities to purpose-design the protein produce and also the production process.” (p. 3) van der Ley et al teaches that the production host can be a bacteria (i.e. commensal *Neisseria*). *E. coli* is the most used bacterium for recombinant DNA technology and has been extensively studied as production host for heterologous proteins (p. 5). The prior art teaches that bacteria other than *E. coli* have been used successfully for the production of recombinant antigens or heterologous proteins (pp. 5-6; Table 3).

Graham et al teaches the method of preparing a composition a polypeptide and a pharmaceutically acceptable carrier. Graham et al teaches that any polypeptide can be used in this method. The prior art teaches that polypeptides prepared by expression in a host cell containing a recombinant DNA molecule, which, comprises a recombinant DNA cloning vehicle or vector (col. 6). The prior art teaches the use of pharmaceutically acceptable carriers (col. 7). The expression of the heterologous polypeptide can be achieved using a range of known techniques and expression systems, including expression in prokaryotic cells such as *E. coli* (col. 8). The prior art also teaches the method of recovering (i.e. isolating) the polypeptide that is produced (col. 8).

Galen teaches the use of plasmid which have been recombinantly engineered to express a variety of expression products (abstract). The prior art teaches the use of plasmids that can be specifically tailored for large-scale protein production, which would include isolating the proteins for use in compositions for example

(col. 9). Heterologous antigens can be expressed within the vector (col. 11).

“The expression plasmids of the present invention preferably express an antigen for presentation to a host to elicit an immune response ...” (col. 19) Galen teaches that any antigen (i.e. heterologous gene product) can be expressed in the bacterial vector (col. 19; col. 21). The host cell can be a bacteria such as *E. coli* or *Salmonella* (col. 25).

Blake et al teaches a method for the high level expression of the outer membrane protein meningococcal group B porin proteins and that the protein is expressed in a bacterium (abstract; cols. 3-4; col. 8; examples). Blake et al teaches methods of isolating the protein product and that the protein can be used in vaccine compositions comprising the protein and a pharmaceutically acceptable diluent, carrier or excipient (col. 4).

It would have been obvious to a person of ordinary skill in the art to use a bacterium, which includes a commensal *Neisseria*, in a method of preparing a composition. The prior art teaches that bacteria are used as host for expressing and producing heterologous proteins and isolating these proteins for use in a composition. The prior art teaches that any gene product (i.e. protein) can be expressed in this manner; thus specific use of outer membrane proteins or any other protein would have been obvious to a person of ordinary skill in the art at the time the invention was made. The protein has been expressed and isolated from the cells and choosing the particular size of protein desired from the protein fraction would have been obvious to a person of ordinary skill in the art at the time the invention was made. The claimed invention is *prima facie* obvious in view of the cited art, absent any convincing evidence to the contrary.

9. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is vague and indefinite in the recitation of "and fragment thereof". It is not clear if this phrase is intended to apply to all of the members of the Markush group or specifically to an outer membrane protein. Can each one of the Markush members have a fragment thereof?

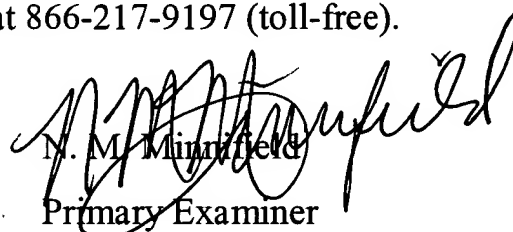
10. No claims are allowed.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



N. M. Minnifield
Primary Examiner

Art Unit 1645

NMM

May 25, 2005